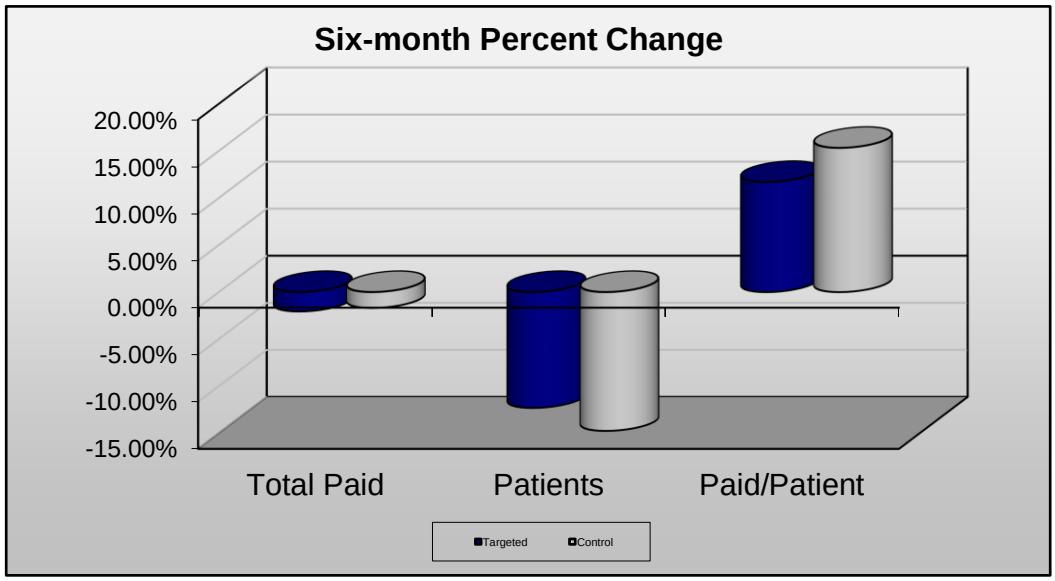
Nonsteroidal Anti-inflammatory Drug Management
Prepared for Texas Medicaid in February 2021

EXECUTIVE SUMMARY

Purpose of Intervention	The goal of this quality management program is to promote safe, cost-effective use of both COX-2 inhibitors and non-selective nonsteroidal anti-inflammatory drugs (NSAIDs).

Intervention	Intervention Type	Population-based mailing
	Intervention Mailing Date	June 24, 2020
	Pre-intervention Period (Baseline)	Jan 2020 – July 2020
	Post-intervention Period (Post)	August 2020 – Jan 2021
	Number of Letters Mailed	105
	Number of Targeted Physicians	105



Savings Calculation

State Cost Savings Calculation:	
Targeted Group: Actual NSAID Management Drugs Average Cost Per Patient Per Month (Pre)	$19.10
% Change in Control Group from Pre to Post	15.32%
Estimated NSAID Management Drugs Paid Amount Per Targeted Patient Per Month if No Intervention	$22.03
Targeted Group: NSAID Management Drugs Cost Per Patient Per Month (Post)	$21.34
Estimated Cost Savings Per Patient Per Month	$0.69
Total Monthly Number of Targeted Panel Patients Served in Post Period	7,821
6-Month Total Savings	$5,396.49
6-Month State General Revenue Funds Savings	$2,159.14
12-Month Total State Savings	$4,318.27

BACKGROUND

NSAIDs are one of the most commonly prescribed classes of drugs. They are more on the radar today in light of the opioid crisis and providers using non-opioid pain alternatives. Gastrointestinal (GI) problems are the most common side effects associated with NSAID use. NSAID-induced GI toxicities are a significant cause of morbidity and mortality in the U.S. and have a significant economic impact. NSAIDs have also been associated with increased cardiovascular risk. The Texas Medicaid Fee-For-Service Program spent $378,901 on NSAIDs this past year.

Indicator #1: Increased Risk of Adverse Drug Events: NSAID-Induced GI Toxicity

NSAIDs are one of the most commonly prescribed classes of drugs. Gastrointestinal (GI) problems are common side effects associated with NSAID use[1-3] A boxed warning for all NSAIDS highlights gastrointestinal risk with these agents (Appendix-Table 1).[4]
The following are documented risk factors for NSAID-using patients and GI toxicity: age > 60, high dose NSAID, concurrent use of steroids, oral anticoagulants, or aspirin (>325mg/day), and prior history of a GI event. [1-3]
NSAID discontinuation is the most effective method for reducing GI toxicity risk. Initiating prophylactic treatment in all patients requiring NSAIDs may be unnecessary and cost-prohibitive but may be considered for high risk patients due to the substantial morbidity and mortality associated with NSAID-induced GI complications. [1-3]

Candidates (denominator):	Patients receiving a non-selective NSAID in the past 90 days for at least 35 days duration
Exception Criteria (numerator):	Candidates with any of the following risk factors: • Concurrent warfarin use • Concurrent steroid use • Concurrent aspirin use (≥81mg) • High dose NSAID (>75% maximum recommended daily dose) • History of GI event (PUD or GI bleed diagnosis) • Age > 60 years

Indicator #2: Use of COX-2 Inhibitors in the Absence of Risk Factors for GI Toxicity

Non-selective NSAIDs and selective COX-2 inhibitors are reported to have equal analgesic efficacy. Use of selective COX-2 inhibitors in the absence of risk factors may not be cost-effective since COX-2 inhibitors are more expensive than generic non-selective NSAIDs. [1]

Candidates (denominator):	Patients receiving COX-2 inhibitors within the past 60 days.
Exception Criteria (numerator):	Candidates without any of the risk factors listed in indicator #1, and without any of the following: inferred rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis, juvenile idiopathic arthritis, pain relating to dysmenorrhea, and/or therapeutic failure of a non-selective

NSAID product.

Indicator #3: Increased Risk of Adverse Drug Events: NSAID Use and Recent Myocardial infarction

According to guidelines from the American Heart Association, patients taking NSAIDs (selective and non-selective products) before a myocardial infarction (MI), should have those agents discontinued at the time of the presentation with MI because of the increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use.[4,5]

Candidates (denominator):	Patients with a myocardial infarction in the past 6 months who have Rx claims for an NSAID product in the past 45 days.
Exception Criteria (numerator):	Candidates who have not been on more than 1 NSAID in the past year, who have at least 120 days of therapy with the NSAID in the past 180 days, and who have claims history for an NSAID product in the time period of 6 months to one year previous.

Indicator #4: Increased Risk of Adverse Drug Events: NSAID and Bisphosphonate

Since NSAIDs and bisphosphonates are associated with gastrointestinal irritation, caution should be exercised in the concomitant use of NSAIDs with these agents.[6,7] The bisphosphonates include risedronate (Actonel), alendronate (Fosamax), and ibandronate (Boniva).

Candidates (denominator):	All patients receiving a NSAID or COX-2 inhibitor within the past 45 days.
Exception Criteria (numerator):	Candidates receiving an interacting drug (bisphosphonate) concurrently, who are not already on a proton pump inhibitor or misoprostol.

Indicator #5: Increased Risk of Adverse Drug Events: NSAID-Induced GI Toxicity in patients with Tobacco or Alcohol Use

NSAID discontinuation is the most effective method for reducing GI toxicity risk. Tobacco and alcohol use have been reported to increase the risk of NSAID-induced ulcers in some studies although the reported relationships between these factors are inconsistent.[3]

Candidates (denominator):	All patients receiving a NSAID or COX-2 inhibitor within the past 45 days.
Exception Criteria (numerator):	Candidates with history of tobacco or alcohol abuse in the last 180 days either by medical diagnosis or inferred drug therapy with the following medications: nicotine replacement therapy, bupropion (Zyban®), varenicline, acamprosate, disulfiram, or

naltrexone.

Indicator #6: Therapeutic Duplication: Concurrent Use of >1 NSAID

Multiple NSAIDs should not be used concurrently due to increased risk of GI adverse effects and lack of evidence of increased efficacy.

Candidates (denominator):	All patients receiving an NSAID product within the past 45 days
Exception Criteria (numerator):	Candidates receiving > 1 NSAID product concurrently are identified.

Indicator #7: NSAID use in Patients with Cardiovascular Risk

A boxed warning for all NSAIDs highlights risks of serious cardiovascular thrombotic events, myocardial infarction, and stroke (Table 1).[4] Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. Alternative treatments should be considered and the risk/benefit be reviewed for NSAID use.[1]

Candidates (denominator):	All patients receiving an NSAID or COX-2 inhibitor for > 90 days in the last 150 days
Exception Criteria (numerator):	Candidates with a documented (i.e., diabetes, hyperlipidemia, arthrosclerosis, post MI, peripheral vascular disease, cerebral atherosclerosis, angioplasty, stent placement, CABG, or artherectomy) or inferred (i.e., > 2 prescriptions for either nitroglycerin or pentoxifylline use in the last 180 days) history of cardiovascular disease.

Indicator #8: NSAID use in Patients with Congestive Heart Failure

According to the 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Diagnosis and Management of Chronic Heart Failure in the Adult, NSAIDs should be avoided in patients with CHF since their use can lead to an exacerbation of heart failure symptoms.[8] Additionally, the use of NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended in the management of CHF.

Candidates (denominator):	All patients receiving an NSAID or COX-2 inhibitor in the last 45 days
Exception Criteria (numerator):	Candidates with a history of congestive heart failure in the last 730 day, AND Candidates with a history of congestive heart failure in the last 730 days and a hospitalization or emergency room visit with a primary diagnosis of congestive heart failure in the last 365 days, AND Candidates with a history of both congestive heart failure and hypertension in

the last 730 days, AND Candidates with a history of both congestive heart failure in the last 730 days and renal impairment in the last 365 days.

METHODOLOGY

In June 2020, all physicians treating patients with any of the aforementioned drug-related problems were identified. Based on the distribution of patients/physician, the minimum patient/month threshold was set at one or more patients (i.e., physicians with one or more patients having a drug-related problem received the mailing). Providers were mailed the intervention materials on June 24, 2020.

Operational definitions:

Targeted Group – physicians treating three or more patients or more patients with any of the aforementioned drug-related problem(s) and who received mailed intervention materials *(Section 1.e.1.A Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Control Group - physicians treating patients taking an NSAID but did not receive mailed intervention materials *(Section 1.e.1.A Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Intervention Drugs – Non-Steroidal Anti-inflammatory Drugs

Pre Intervention Time Period – Jan 01, 2020 through June 30, 2020

Post Intervention Time Period – August 01, 2020 through January 31, 2021

6-month Total Paid – total drug costs can be defined as the total amount of paid NSAID drug claims for the above time periods for the prescribers in the control and target groups. The target group consisted of those prescribers who had prescribed NSAID drug therapy to more than two Medicaid patients. The control group consisted of all other prescribers who prescribed NSAID drug therapy agents in the designated time periods *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Average Number of Panel Patients per Month - during the 6-month pre and post time periods, the number of unique Medicaid patients with a drug claim submitted using a respective provider number was captured each month. Medicaid patients that did not have a drug claim were not counted in the prescriber's panel. The monthly numbers were summed then divided by six to calculate the monthly average. For example, in Table 3, the physician (with provider number AB123456) had an average of 12 patients with at least one drug claim per month. If a patient had two different claims in June, they would be counted as one patient. By evaluating all patients seen by a specific physician, changes in prescribing patterns can be evaluated on existing and new patients *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

Table 3: Average Number of Panel Patients per Month

Provider Number	Month #	Number of Unique Patients with a Drug Claim
AB123456	1	10
	2	10
	3	10
	4	12
	5	13
	6	17
Total		72
Average Number of Panel Patients per Month		12

Average Cost/Patient per Month – this was calculated by dividing the total dollars paid for drug claims during the analysis time period by the total number of Medicaid panel patients during the respective time period. For example, in the targeted group post analysis; there were 7,821 patients who had a drug claim during the six-month review period. The total amount of dollars paid for drug claims for these patients during the post analysis was $166,891. Dividing these two numbers ($166,891/7,821) yields an average cost per patient of $21.34 *(Sections 1.e.1. and 1.e.2 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal).*

$$\textbf{Average Cost/Patient/per Month} = \frac{\textbf{6-month Total Amount Paid for NSAID Drugs}}{\textbf{Average number of Panel Patients per Month}} / \textbf{(\# Months)}$$

Total State Savings *(Sections 1.e.3 and 1.e.4 Exhibit A of the Agreed Modifications to the RFP and Contractor Proposal)***:**

- Intervention Average Cost Savings per Month - the percent change seen in the control group was applied to the intervention group baseline Average Cost per Patient per Month. This amount represents the estimated Amount Paid per Targeted Physician per Patient in the absence of the intervention (i.e., Estimated Paid Amount). The Estimated Paid Amount per Patient per Month was then subtracted from the actual Intervention Target Group Average Cost per Patient per Month to estimate the Average Cost Savings per Patient per Month.
- 6-Month Total Savings - the Intervention Average Cost Savings per Patient per Month was multiplied by the total number of targeted patients served over the 6-month time frame.
- 6-Month State General Revenue Funds Savings= 6-Month Total State Savings X 0.4001.
- Total State Savings = 6-Month State General Revenue Funds Savings X 2.

RESULTS

Population-based intervention

A total of 105 physicians were targeted and received intervention materials. Table 4 compares the 6-month total amount paid for NSAID drugs, the total number of patients in each physician's panel per month, and the average cost per patient for the targeted and control groups during the six-month pre and post periods. When comparing the pre-Average Cost per Patient per Month between the targeted and control groups, the cost was approximately $21 higher for the control group. This difference may be due to such factors as the targeted group having more patients prescribed NSAIDs per physician or that associated average NSAID drug costs are inherently higher in the targeted group.

The control group saw a 1.69% decrease in the amount paid for intervention-related drugs while the targeted group saw a 2.06% decrease. Additionally, the average number of monthly patients for the physician's panel decreased 12.31% for the target group and decreased 14.75% for the control group. To control for changes in case load variance (i.e., the change in the number of panel patients) between the two groups, the average cost per patient was also calculated. Total amount paid and number of panel patient trends led to a 11.69% increase in average cost per patient per month in the targeted group and a 15.32% increase for the control group.

Group	NSAID Drugs -- Six Months Total Paid Pre/Post			Average Number of Panel Patients per Month			NSAID Drugs Average Cost per Patient per Month		
	Pre	Post	Change	Pre	Post	Change	Pre	Post	Change
Targeted	$170,396	$166,891	-2.06%	1,487	1,304	-12.31%	$19.10	$21.34	11.69%
Control	$39,827,012	$39,155,665	-1.69%	165,227	140,858	-14.75%	$40.17	$46.33	15.32%

Table 4: Six-Month Trends for Overall Targeted vs Control Group

Table 5 shows the Intervention Average Cost Savings per Patient per Month and the savings calculations. Had the intervention not been mailed, the targeted pre average cost per patient per month would have increased 15.32% from $19.10 to $22.03. The net difference between the actual and estimated average cost/patient for the targeted group was $0.69. Based on 7,821 targeted patients served per month during the six-month post period, the six-month Total Savings and Total State Savings were $5,346.49 and $2,159.14 respectively. Over a twelve-month period, the Total State Savings was $4,318.27.

Table 5: Overall Intervention Average Cost Savings

State Cost Savings Calculation:	
Targeted Group: Actual NSAID Management Drugs Average Cost Per Patient Per Month (Pre)	$19.10
% Change in Control Group from Pre to Post	15.32%
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Table 6 shows the changes in the clinical indicators based on the intervention. The overall change in indicators is a decrease of 32.7%.

Table 6: Overall Intervention Changes in Clinical Indicators

Clinical Indicators	Baseline	Jan-2021	% Change
Identify patients at risk of adverse events, with factors that can increase GI toxicity: NSAIDs and GI toxicity	17	12	-29.4%
Identify patients at risk of adverse events, with factors that can increase GI toxicity: NSAIDS with tobacco or alcohol use	65	47	-27.7%
Reserve use of a COX-2 inhibitor for patients with risk factors for GI toxicity	2	1	-50.0%
Recognize patients with concurrent use of >1 NSAID	1	0	-100.0%
Evaluate NSAID use in patients with cardiovascular risk	9	5	-44.4%
Reconsider NSAID use in patients with congestive heart failure (CHF)	16	9	-43.8%
Total	110	74	-32.7%

CONCLUSIONS

This population-based intervention was successful in encouraging appropriate use of drug therapy and providing prescribers with educational tools to better communicate with their patients' issues regarding appropriate treatment. This resulted in an economic impact on Texas Medicaid's pharmacy program expenditures, with a calculated twelve-month overall savings of $10,792.98 and savings to the State of $4,418.27 and a decrease in clinical indicators of 32.7%.

REFERENCES

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Appendix

Table 1: NSAID Black Box Warning[4]

Boxed Warning for all NSAID Products
Cardiovascular Risk • NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk . • NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. **Gastrointestinal Risk** • NSAIDS cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.